REMARKS

Favorable reconsideration of this application is requested in view of the following remarks.

Claims 41 and 43-48 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Beckert et al. (International Application Publication No. 02/060415), to which English equivalent U.S. Patent Application Publication No. 2003/0152627 is referred, in view of Kelm et al. (U.S. Patent No. 5,656,290). Applicants respectfully traverse this rejection.

Beckert discloses a multiparticulate drug including pellets A and B (see abstract) and further discloses that pellet B releases less than 20 % of an active ingredient at pH 6.8 after 4 hours and 6 hours (see abstract, paras. [0015] on page 1and [0046] on page 3, and claim 1 of the US '627 reference, and hereinafter, cited paragraphs are those of the US '627 reference). It seems from the abstract and claim 1 of the reference that the disclosure of "not more than 20...% of the active ingredient after 4 hours" in paragraph [0046] of the reference could be an inadvertent error and could be "in 6 hours". As shown in Fig. 1 of the attached Declaration of Mr. Takashi KURASAWA, who is one of the inventors of the present application, composition (i) of claim 41, i.e., Granule H in the Declaration, dissolves at pH 6.8 almost 100 % in 6 hours and more than 30 % in 4 hours. Further, in Fig. 1 of the Declaration of Mr. Kurasawa, composition (ii) of claim 41, i.e., Granule L-S, dissolves at pH 6.8 almost 100 % in 2 hours. Thus, composition (ii), which is soluble at lower pH than 6.8 such as pH 5.0-6.0, included in the capsule of claim 41 releases the active ingredient rapidly at pH 6.8, i.e., in a pulse mode (see Fig. 1 of the Declaration). The reference, however, discloses that the active ingredient included in pellets A having an inner polymer coating is released at pH 6.8 about 40-70 % of an active ingredient in 2 hours and 60-100 % in 4 hours (see para. [0024] on page 2). Thus, there is no reasonable basis to assume that the pellet A of the reference dissolves sufficiently at pH 5.0-6.0 as claim 1 recites. Further, the composition (i) of claim 41 dissolves at pH 6.0-7.5, and dissolves completely at pH 6.8 in 6 hours (see Fig. 1 of the Declaration). The reference, however, discloses that not more than 20 % of the active

ingredient in pellet B is released at pH 6.8 after 6 hours (see abstract and para. [0015] on page 3). Thus, the reference does not teach or suggest the compositions (i) and (ii) of claim 41, which provide the particular release profile of the active ingredient, as discussed above.

Further, as shown in table A in the Declaration, the plasma level of the active ingredient of claim 41, i.e., lansoprazole, released in beagle dogs is maintained in a therapeutically effective level over a long period of time after capsules of claim 41 including the compound are administered orally to the dogs. In addition, table A shows that the plasma level after 1 hour from the administration of lansoprazole is less than those measured after 2 hours and 3 hours from the administration, and a spike-like peak immediately after administration is not observed (see the Declaration) even though composition (ii) of claim 41 releases the active ingredient in a relatively short period of time (see Fig. 1 of the Declaration). Moreover, Beckert, which discloses the release patterns of the active ingredient in pellets A and B in vitro as discussed above (see para. [0024] on page 2 and [0046] on page 3), does not disclose a plasma level profile of any active ingredient in the drug in vivo like that of table A of the Declaration. It is known in the art that the plasma level profile varies in vivo and does not necessarily correspond to the release patterns of the active ingredient in vitro because the profile is influenced by a process of absorption of a dissolved active ingredient, distribution, metabolism, and excretion thereof as well as the preparation method of the composition. Accordingly, the long-maintained therapeutically effective plasma level without a spike-like peak immediately after the administration obtained by the capsule of claim 41, which includes composition (ii) that releases the active ingredient in a short period of time as discussed above, is unexpected from the disclosure of Beckert.

Kelm discloses a pharmaceutical composition including bisacodyl as an active ingredient, which is released near an inlet to or within a colon (see abstract). Bisacodyl is a laxative and the only active ingredient disclosed in the reference. The composition of Kelm controls the release of bisacodyl by using two or more enteric coating layers (see abstract). In contrast, the capsule of claim 41 includes two granule compositions. Thus, the reference does not disclose the capsule of claim 41 including two compositions (i) and (ii), which provides the particular release patterns of the active ingredient in vitro at

pH 6.8 and maintains therapeutically effective plasma level of the active ingredient for the long period of time without the spike immediately after administration of the capsule as discussed above (see Fig. 1 and table A of the Declaration). Further, it is known that an indication, a mode of action, and the target of laxatives are quite different from those of the imidazole compounds of claim 41. Thus, Kelm does not teach or suggest the capsule including compositions (i) and (ii) including the imidazole compound (I') of claim 41, and the reference does not remedy the deficiencies of Beckert.

Accordingly, claim 41 and claims 43-48, which ultimately depend from claim 41, are distinguished from Beckert in view of Kelm, and this rejection should be withdrawn.

Claim 42 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Beckert et al. (International Application Publication No. 02/060415) in view of Kelm et al. (U.S. Patent No. 5,656,290), and further in view of Karehill et al. (International Patent Application Publication No. 99/32091). Applicants respectfully traverse this rejection.

Claim 42, which depends from claim 41, is distinguished from Beckert in view of Kelm for at least the same reasons as discussed for claim 41 above.

Karehill discloses a pharmaceutical composition including a proton pump inhibitor, which provides extended release for 2-12 hours (see "Field of invention" on page 1). Karehill, however, neither discloses the capsule including two compositions (i) and (ii) as claim 41 recites nor the particular release patterns of the active ingredient in vitro at pH 6.8 of the compositions (i) and (ii) in vitro nor the moderate plasma level change of the active ingredient after administration in vivo such as those obtained from the compositions of claim 41 as discussed above for Beckert. Thus, Karehill does not remedy the deficiencies of Beckert and Kelm, and claim 42 is distinguished from Beckert in view of Kelm, and further in view of Karehill. Accordingly, this rejection should be withdrawn.

Claim 49 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Beckert et al. (International Application Publication No. 02/060415) in view of Kelm et al. (U.S. Patent No. 5,656,290), and further in view of Yamamoto et al. (U.S. Patent No. 5,264,223). Applicants respectfully traverse this rejection.

Claim 49, which depends from claim 41, is distinguished from Beckert in view of Kelm for at least the same reasons as discussed for claim 41 above.

Yamamoto discloses a hard capsule for pharmaceutical drugs including water-soluble cellulose derivatives, etc. (see abstract). Yamamoto, however, neither discloses the capsule including two g compositions (i) and (ii) as claim 41 recites nor the particular release patterns of the active ingredient in vitro at pH 6.8 of the compositions in vitro nor the moderate plasma level change of the active ingredient after administration in vivo such as those obtained from the compositions of claim 41 as discussed above for Beckert. Thus, Yamamoto does not remedy the deficiencies of Beckert and Kelm, and claim 49 is distinguished from Beckert in view of Kelm, and further in view of Yamamoto. Accordingly, this rejection should be withdrawn.

In view of the above, Applicants request reconsideration of the application in the form of a Notice of Allowance.

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